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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,270	HAGEMAN ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,10,11 and 21-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,10,11 and 21-31* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/07/2005 has been entered. An action on the RCE follows.

2. Claims 1, 2 and 10 have been amended. Claims 23-31 have been added. Therefore claims 1-5, 10, 11 and 21-31 are pending and under consideration.

3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101, withdrawn

4. The rejection of claims 1-5, 10, 11 and 22 under 35 USC § 101, as lacking utility is withdrawn because of Applicants persuasive argument and art evidence provided in the response of 9/7/05.

Claim Rejections - 35 USC § 112, first paragraph, withdrawn

5. The rejection of claims 1-5, 10, 11 and 22 under 35 USC § 112, first paragraph, as lacking enablement is withdrawn because of Applicants persuasive argument and art evidence provided in the response of 9/7/05.

Claim Rejections - 35 USC § 102(b), withdrawn

6. The rejection of claims 1-3, 10 and 11 under 35 USC § 102(b), as being anticipated by Bonaldo et al. (1996) is withdrawn because Applicants have provided documentation

to indicate that this sequence was not available to the public till 2/28/02 (after the instant filing date 11/6/2001).

Claim Objections

7. Claim 26 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 recites a fragment to include 750 nucleotides, however, claim 26 recites a fragment size of only 500 nucleotides..

Claim Rejections - 35 USC § 112 (New)

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8a. Claims 1-5, 10, 11 and 21-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the nucleotides of SEQ ID NO: 1 and nucleotides encoding SEQ ID NO: 2 (Page 10, paragraph 47). This meets the written description provisions of 35 USC 112, first paragraph. However, the specification does not disclose all possible fragments of SEQ ID NO: 1, including those that are at least 95% identical

to SEQ ID NO: 1 or a nucleotide sequence encoding a polypeptide fragment of 190 contiguous amino acid residues of SEQ ID NO: 2 or primers or probes or the complements of these sequences contemplated by the Applicant. The claims as written, however, encompass SEQ ID NO: 1 variant sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1, 2, 4 and 21-31. The specification does not provide written description to support the genus encompassed by the instant claims.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to polynucleotides having at least 95% sequence identity with a particular disclosed sequence (fragments), or that is complement to a disclosed sequence. The claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. The specification teaches that PRO731 has (unspecified) homology to secreted and transmembrane polypeptide. The structure of the putative human IPM 150 is disclosed on page 10, paragraph 47 of the specification, as having a signal peptide corresponding to amino acids 1-20, a NH-terminal domain, corresponding

to about amino acids 71-88, conserved domain 1 corresponding to amino acids 95-115, conserved domain 2 corresponding to amino acids 575-646, and EGF like domain corresponding to amino acids 688-731 respectively. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity or fragment length. There is not even identification of any particular portion of the structure that must be conserved for function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated polynucleotide of SEQ ID NO: 1 and polynucleotide encoding SEQ ID NO: 2, the skilled artisan cannot envision all the detailed chemical structure of the claimed nucleotide sequences of the fragments regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated polynucleotide of SEQ ID NO: 1 and polynucleotide encoding SEQ ID NO: 2 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Claims 3, 5, 10 and 11 are rejected insofar as they are dependent on claims 2 and 4. As a result, it does not appear that the inventors were in possession of various polynucleotide sequences set forth in claims 1-5, 10, 11 and 21-31.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

8b. Claims 1-5, 10, 11 and 21-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for SEQ ID NO: 1 and polynucleotides encoding SEQ ID NO: 2 as described in Page 10, paragraph 47, does not reasonably provide enablement for all possible possible fragments of SEQ ID NO: 1, including those that are at least 95% identical to SEQ ID NO: 1 or a nucleotide sequence encoding a polypeptide fragment of 190 contiguous amino acid residues of SEQ ID NO: 2 or primer or probe or the complements of these sequences contemplated by the Applicant. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not provide working examples of different DNA sequences that would enable a representative number of the above discussed DNA sequences with assurances that they can be used to encode the protein of interest. The mere recitation of the size, and the definitions provided do not serve as sufficient guidance to enable the breadth of the claims for the various DNA sequences claimed. See Ex parte *Forman*, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C. 112 requires that there must be an enabling disclosure to support the breadth of the claims, a review of the specification confirms that the scope of the various DNA sequences that are discussed above have not been enabled. There is but a single polynucleotide disclosed with reference to IPM150 isoform A, SEQ ID NO: 2. In the absence of

working examples, breadth of claims and sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims. The breadth of the claims includes polynucleotides of as little as 12 nucleotides. With these points in mind, it is the Examiner's position that giving the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement without undue experimentation because of the breath of claims, the lack of guidance provided and the quantity of experimentation needed to make or use the invention.

Since the claimed polynucleotides are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification asserts that IPM150 is an inter photo receptor matrix polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function. The structure of the putative human IPM 150 is disclosed on page 10, paragraph 47 of the specification, as having a signal peptide corresponding to amino acids 1-20, a NH-terminal domain, corresponding to about amino acids 71-88, conserved domain 1 corresponding to amino acids 95-115, conserved domain 2 corresponding to amino acids 575-646, and EGF like domain corresponding to amino acids 688-731 respectively. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function.

Despite knowledge in the art for producing variants of a given polypeptide with amino acid deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function of the all-possible allelic variants or splice variants or fragments with activity or modifications claimed in the instant invention. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine,

without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Therefore, predicting which nucleotide sequence encoding the variants would retain the functions of the IPM-150 protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications of the nucleotides contemplated and yet retain the function of the IPM-150 variant proteins claimed. Applicants have not taught how one of skill in the art would use the full scope of polynucleotide sequences encompassed by the invention of claims 1, 2, 4 and 21-31. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences.

Given the breadth of claims 1, 2, 4 and 21-31 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 3, 5, 10 and 11 are rejected insofar as they are dependent on claims 2 and 4. Therefore, claims 1-5, 10, 11 and 21-31 remain rejected because Applicants have not taught how one of skill in the art would use the full scope of polynucleotide sequences encompassed by the invention.

8c. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-31 recites the limitation "exactly complementary" in the claims. It is the examiners understanding that the complementary sequences by definition are "exact". The specification fails to define the terms so as to set forth the meets and bounds of the invention.

9. Claims 3, 5, 10 and 11 would be allowable if rewritten to include all the limitations of the base claims from which they depend.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSS 1/06

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER